September 18, 1958

Dr. P. R. Edwards
Communicable Disease Center
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Chamblee, Georgia

Dear Phil:

Thank you for your recent letters which I am attending to on the heels of my return to Madison.

A propos the Postal Department's proposed rules I am of course as deeply concerned as you predicted I would be and have written the enclosed letter accordingly. Thank you for bringing this to my attention.

We may be moving further from Georgia than we are now but I hope our new situation can attract you to visit us more often than you have been able to in the past. There is no thought of disbanding any laboratory and there is every prospect of the continuation and strengthening of the type of research we have been doing so far.

I am not sure what might be going wrong in your transduction experiments and can only offer the following guesses:

1. You are certainly using a tremendously larger total volume of material than I would think would be necessary. Our standard mixtures for selection of motile transductions would contain perhaps one tenth of .1 ml of a grown broth culture of a bacterium mixed with an equal volume of the high titered bacteriophage lysate. In a cleanly working system such a setup should give you many hundreds or thousands of motile clones per sample. Just possibly you are using a higher density of bacteria in the suspension than may be necessary. Since your innoculum is bound to grow out to a final average density no matter how few you put in, it might pay to reduce the input. We have often done very well by simply streaking medium sized loopfuls of the phage bacteria mixture indicated so that we were probably using no more than .01 ml per plage. For more difficult combinations we might use as much as .1 ml innoculated into the top of a motility tube. I don't see any special point in doing the incubation for adsorption because I don't think you will prevent adsorption by adding the agar later on. Nor can I see any harm in it. By and large your procedure seems to me perhaps overelaborate and I would simply take a drop or so of the mixture and innoculate it into the top of a motility tube.

2. A more likely reason for difficulty may be the nonadaptation of your phage to paratyphi B. It is reasonably possible that you would get better results using phage that has been grown on other strains, for example, SW 666 or other B strains. However if you are getting good lysis of your recipient culture this is probably not the answer. It might pay to try to lysogenize the recipient first before attempting the transduction experiment although this is a little far fetched.

3. Finally you may simply be dealing with a nonmotile culture which, like Salmonella pullorum, has multiple defects in motility. Since only one plus factor is likely to be transduced at a time this could give you a refractory recipient.

All I can say with regard to all of these points is suggest that you try your luck with a system that has been well worked over before, for example, Salmonella typhimurium TM 2 -- x SW 666 or some other standard nonmotile recipient.

This is certainly no bother and I hope you will let me know if you get over the present troubles.

With all best regards.

Yours sincerely,

Joshua Lederberg
Professor of Medical Genetics